

REMARKS

Applicants thank the Examiner for the thorough consideration given the present application.

Claims 1-2, 4, 9-27, 29, 31 and 32 are pending. Claim 1 is amended. Claims 3, 5-8, 28 and 30 were previously cancelled. Claim 32 is added. No new matter is added. For instance, amended claim 1 finds support in the Examples of the instant specification and Fig. 2B. Also, new claim 32 is supported by Table 1 of the instant specification. Thus, no new matter has been added.

In view of the below remarks, the Examiner is respectfully requested to reconsider the pending application, as amended.

Issue under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1, 2, 4, 26, 27, 29 and 31 under 35 U.S.C. §112, second paragraph for the reasons recited at page 4 of the outstanding Office Action. Applicants respectfully traverse this rejection.

Claim 1 is amended to remove reference to “poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 1,000,000 or more.” By way of the present submission, this rejection is moot. Therefore, reconsideration and withdrawal thereof are respectfully requested.

Issue under 35 U.S.C. §112, first paragraph (new matter)

The Examiner has rejected claims 1, 2, 4, 26, 27, 29 and 31 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Examiner indicates at page 5 of the Office Action that

Claim 1, upon which claims 2, 4, 26, 27, 29 and 31 depend, recites gels spots that "have a spherical shape of three-dimensional structure" in line 3. While Example 3 of the instant specification discusses spots having "most excellent three dimensional structure," a review of the specification yields no teaching of spots having "spherical shape or structure; therefore, the recitation of spots that have a "spherical" shape constitutes new matter.

While not conceding to the Examiner's rejection, in an effort to advance prosecution only, claim 1 is amended to change "spherical shape of three-dimensional structure" to "hemispherical shape of three-dimensional structure".

Applicants respectfully direct the Examiner's attention to the Examples of the instant specification and FIG. 2B. Specifically, the step of Example 2 explains that the sol mixture prepared in step 2 was integrated into circular spots having a diameter of 100 to 500 μ m on the slide. Also, Example 3 discloses formation of spots with the most excellent three dimensional structure, as also recognized by the Examiner. Further, FIG. 2B illustrates a photograph of a spot having hemispherical shape in the biochip prepared according to Example 4.

Therefore, it is evident that the disclosure of the instant specification implicitly discloses a gel spot having "hemispherical shape of three-dimensional structure". Thus, Applicants respectfully submit that the presently amended term is supported by the instant specification. If the Examiner still believes that this language is inappropriate, Applicants request that the Examiner contact Applicant's representative to discuss this issue in detail and advance prosecution.

As discussed above, the present rejection is moot and reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. § 103(a)

The following rejections are pending:

- (1) Claims 1, 2, 26 and 27 are rejected under 35 U.S.C. § 103(a) as being obvious over Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001)) in view of Avnir et al. (USP No. 5,292,801) in view of Simon et al. ((USP No. 5,569,607).
- (2) Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Avnir and in view of Simon and further in view of Malhorta (USP No. 5,624,743).
- (3) Claims 27 and 29 are rejected under 35 U.S.C. 103(a) as being obvious Kim in view of Avnir and in view of Simon and further in view of Croxson (USP No. 5,108,891).
- (4) Claim 31 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Avnir and in view of Simon and further in view of Maracas (USP No. 5,725,788).

Applicants respectfully traverse these rejections.

While not conceding to the Examiner's rejections, claim 1 is amended to further emphasize the distinctions between the present invention and the cited references.

The Present Invention

Claim 1 of the present invention is directed to a biochip, comprising: a chip substrate; circular porous gel spots mounted and immobilized on said chip substrate, wherein said gel spots have a hemispherical shape of three-dimensional structure and pores therein; and biomaterials entrapped in said pores of said gel spots and encapsulated by said gel spots, and said biomaterials have a free orientation without being covalently bond to the gel, wherein said gel spots are glassy gel formed by the gelation of a sol mixture containing: biomaterials; a silicate monomer composed of tetramethyl orthosilicate (TMOS) and methyltrimethoxysilane (MTMS); and at least one additive selected from the group consisting of polyglyceryl silicate (PGS), 3-glycidoxypropyltrimethoxysilane (GPTMOS), (N-triethoxysilylpropyl)-O-polyethylene oxide urethane (PEOU), glycerol and polyethylene glycol (PEG), wherein said chip substrate is

selected from the group consisting of polymethyl methacrylic acid (PMMA), polycarbonate (PC) and cyclic olefin copolymers (COC) and coated with a coating agent selected from the group consisting of polyvinyl acetate (PVAc) having a molecular weight in the range of 800 to 200,000, poly(vinyl butyral-co-vinylalcohol-co-vinyl acetate) having a molecular weight in the range of 70,000 to 120,000, poly(methyl methacrylate-co-methacrylic acid) having a molecular weight of 10,000 or more, poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 200,000 or more, poly(methyl acrylate) having a molecular weight of 10,000 or more, 3-glycidoxypolytrimethoxysilane (GPTMOS), dissolved in solvent(s) selected from the group consisting of methylene chloride, tetrahydrofuran, ethanol, methanol, butanol, methyl ethyl ketone, acetone, isopropyl alcohol, ethyl acetate, methyl isobutyl ketone, and diacetone alcohol, and wherein up to 1,000 spots/cm² are integrated on the chip substrate.

Distinctions over the Cited Art

One embodiment of the present invention requires the biochip based upon the sol mixture composed by combination of the specific silicate monomers and additives and the gel spots of the spherical shape of three-dimensional structure. However, the cited references are silent concerning the claimed combination of features.

As to the Kim Reference

The Kim reference (which is the primary reference utilized in all rejections) fails to disclose or suggest the presently claimed features. Rather, Kim is interested mainly in encapsulation within microchanneled sol-gel networks and thus, focuses on the structure or size of pores suitable for encapsulating biomaterials. Kim does not disclose or suggest at least the claimed feature that, as acknowledged by the Examiner, requires that the gel spots are glassy gel spots. Also, Kim remains silent as to the claimed features that the glassy gel spots have a hemispherical shape of three-dimensional structure and are formed by the gelation of a sol mixture containing biomaterials, a silicate monomer composed of tetramethyl orthosilicate (TMOS) and methyltrimethoxysilane (MTMS) and at least one specific additive selected from the group consisting of polyglyceryl silicate (PGS), 3-glycidoxypolytrimethoxysilane

(GPTMOS), (N-triethoxysilylpropyl)-O-polyethylene oxide urethane (PEOU), glycerol and polyethylene glycol (PEG).

Therefore, the present invention is patentably distinct from the Kim reference. Further, as seen below, the other cited references cannot cure the deficiencies of the Kim reference.

As to the Avnir Reference

The deficiencies of the Kim reference cannot be cured by Avnir for at least the following reasons:

First, the sol mixture according to the present invention is prepared, in part, from a silicate monomer mixture composed of tetramethyl orthosilicate (TMOS) and methyltrimethoxysilane (MTMS) and at least one additive selected from the group consisting of poly glyceryl silicate (PGS), 3-glycidoxypropyltrimethoxysilane (GPTMOS), (N-triethoxysilylpropyl)-O-polyethylene oxide urethane (PEOU), glycerol and polyethylene glycol (PEG).

In contrast, the sol mixture of the Avnir reference is prepared from only TMOS as the silicate monomer, and PEG 400 or PEG 6000 as additives. See the Examples of Avnir. Thus, the claimed combination of features is absent from the cited art. Further, it is impossible to achieve the unexpectedly surprising effects of the present invention by using the sol mixture of the Avnir reference.

In this context, Example 3 of the instant specification describes the combination of the specific silicate monomers and additives, which are able to provide a composition for optimal performance according to types and size of proteins to be immobilized on the protein chip. In other words, the results as set forth in Table 2 of the instant specification show excellent performance when using the combination of the claimed tetramethyl orthosilicate (TMOS) and methyltrimethoxysilane (MTMS) as silicate monomers and the claimed additive (emphasis added).

More specifically, Example 3 of the instant specification illustrates unexpectedly

superior effects in that the specific silicate monomers and additives contribute to the formation of spots with excellent three-dimensional structure. Further, Experiments 3-5 of Example 4 show that the spots formed by the gelation according to the present invention are transparent, have no cracks (Experiment 3), and are stable for more than 6 months (Experiment 4).

Second, the Examiner indicates at page 7 of the Office Action that

The Avnir reference teaches three dimensional shape (e.g., rods, discs, cubes), "in any shape" of the glassy gel spots.

However, the Avnir reference simply discloses at column 3, lines 20-28 that

"The sol gel glass according to the present invention can be in any shape suitable for the test. For example it can have the shape of rods, discs, cubes, sieves, powder, or thin films coating conventional glass plates or any other inert solid support. Thus, an electrochemical test according to the invention can be performed by preparing electrodes coated with doped sol gel glass layers. These electrodes may be used for clinical, analytical or industrial purpose, or as biosensors."

From the above disclosure, it is clear that the Avnir reference simply suggests shapes of sol gel glass suitable for coating electrodes. Indeed, the Avnir reference fails to disclose or suggest a gel spot having "hemispherical shape of three-dimensional structure" according to the present invention. This represents a further distinction.

Additionally, the present invention discloses that the three-dimensional structure allows for the placing of many spots per unit surface area of the slide and after incubation, uniform signal intensity of the encapsulated protein may be observed. Further, the present invention teaches that since the gel spots are not deformed by any outside pressure, the three-dimensional structure can be maintained, thus it is possible to produce a chip with improved sensitivity and to exert superior storage properties. See pages 14-20 of the instant specification. Such results are clearly beyond the ability or contemplation of the cited art.

As to the Remaining Cited References

The deficiencies of Kim and Avnir cannot be remedied by the remaining secondary references including Simon, Malhorta, Croxon and Maracas because they also fail to disclose or suggest the claimed features of the biochip. Therefore, the cited references alone or in combination neither suggest nor disclose the presently claimed biochip.

Consequently, the present invention provides the biochip based upon the sol mixture containing, among others, a combination of the specific silicate monomers and additives. Further, the gel spots have a hemispherical shape of three-dimensional structure. However, the cited references are silent about the aforementioned teachings of the present invention. Thus, the present invention cannot be expected from the cited references individually or in combination.

For the reasons above, since amended independent claim 1 of the present application is believed to overcome the 35 USC § 103(a) rejections, the claims dependent therefrom are also believed to address the same rejections. Therefore, the Examiner is respectfully requested to reconsider and withdraw these rejections.

Conclusion

In view of the above remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie Reg. No. 42,874 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 

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